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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,109	09/15/2003	Youcef M. Rustum	03551.0136	1832

26712 7590 03/09/2005

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,109	RUSTUM ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-11,13 and 14* is/are rejected.

7)☒ Claim(s) *5 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/25/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The following is responsive to the preliminary amendment received Feb. 23, 2004.

No claims are cancelled. No new claims are added. Claims 1-14 are presented for prosecution on the merits.

Information Disclosure Statement(s)

Applicant's Information Disclosure Statement received Feb. 25, 2004 has been considered. Please refer to Applicant's copy of the 1449 submitted herewith.

Claim Objection(s)

1. Claim 1 is objected to because of the following informalities: in claim 1, line 5, before "less", the term "in" should be cancelled and replaced with –is--. Appropriate correction is required.

Claim Rejection(s)—35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 4, 6, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Sieja.

Sieja discloses a clinical trial in which patients suffering from ovarian cancer were treated with cyclophosphamide and cisplatin in combination with selenium (in the form of yeast) (200 micrograms daily). The results of the trial indicate that selenium alleviates

nausea, vomiting, diarrhea, abdominal pain and weight loss. Therefore, Sieja concludes that sufficiently long supplementation with selenium in patients with ovarian cancer subjected to treatment with multi-drug chemotherapy, i.e. cisplatin and cyclophosphamide, results in a reduction in side effects of chemotherapy. Please see pages 958-959.

The claims are anticipated by Sieja because Sieja discloses administration of identical active agents to an individual in need of treatment using Applicant's claimed method steps. Therefore, a reduction in bladder toxicity would be inherent.

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 2, 3, 8-11, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sieja supra in view of Stockel et al., 4,617,189 and El-Bayoumy.

Sieja as applied above.

Sieja does not specifically disclose a method of increasing the therapeutic dose of cyclophosphamide in the patient also receiving selenium supplementation nor does Sieja disclose administration of Applicant's specifically claimed compounds, i.e. seleno-L-methionine and methylselenocysteine.

However, the Examiner refers to Stockel, which discloses a method of negating the toxic effects of platinum compounds used in chemotherapy, wherein the method comprises administering to a patient in need thereof an effective amount (0.6-300 mg) of a selenium compound such as selenomethionine and methylselenocysteine. Stockel additionally discloses that the selenium compounds may be administered prior to treatment to build up levels of selenium in the body to mitigate the toxicity or the selenium compound may be administered concomitant with treatment. Please see col. 3-col. 5.

The Examiner also refers to El-Bayoumy, which teaches that compounds identified in selenium-enriched yeast that have been utilized in human clinical trials are

selenomethionine and Se-methylselenocysteine. Please see page 133, first column, first full paragraph.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the method of Sieja by administering higher than therapeutic doses of cyclophosphamide to the cancer patients because one of ordinary skill in the art would reasonably expect the selenium compound to mitigate any toxicity associated with the higher doses. Such a modification would have been motivated by the reasonable expectation of aggressively treating the cancer while providing some comfort to the patient through the mitigation of the toxic side effects.

With respect to the administration of seleno-L-methionine and methylselenocysteine, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer these specific compounds to the cancer patients in Sieja because (1) since Sieja teaches that selenium is effective in reducing toxicity associated with cyclophosphamide and cisplatin and (2) Stockel et al. disclose that these selenium compounds would be effective in negating the toxicity of platinum compounds such as cisplatin, one of ordinary skill in the art, absent evidence to the contrary, would reasonably expect these selenium-containing compounds to be equally effective in reducing the toxic side effects in the cancer patients receiving cisplatin and cyclophosphamide.

Moreover, El-Bayoumy teaches that selenium-enriched yeast, like the selenium yeast administered to patients in Sieja, contains the compounds selenomethionine and methylselenocysteine (please refer to page 133). Thus, the administration of these

compounds would have been obvious in the method of Sieja, which teaches administration selenium-enriched yeast to the cancer patients.

With respect to claim 13, one of ordinary skill in the art, based on the teachings of the prior art, would reasonably expect the selenium compounds to mitigate any toxicity to the bladder.

Claims 5 and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 1-4, 6-11, 13-14 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
March 6, 2005

Cybille Delacroix-Muirheid
Patent Examiner Group 1600